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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/159,172	09/23/98	ENNIS	F UMMC98-13

HM22/0418

DAVID E BROOKS
HAMILTON BROOK SMITH AND REYNOLDS
TWO MILITIA DRIVE
LEXINGTON MA 02173-4799

EXAMINER	
SAUNDERS, D	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

09/159,172 09/23/98

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/16/01

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9, 11-20 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-9, 11-20 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

The claims pending and under examination are 1-20.

Claims 1-10 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear as to whether step d) is to be carried out unconditionally or only in the case in which the vaccine has been determined in step c) as being capable of stimulating a T-Cell response. It is believed applicant intends the latter; see specification page 4, lines 9-11 and page 8, lines 21-23.

Claim 18 is unclear as to whether step d) is to be conducted unconditionally or only in the case in which the response measure in step c) is greater than the preselected value. It is deemed applicant intends the latter; see page 7, lines 26-28.

Claim 20 is unclear as to what the "autologous cells" are autologous with -- the T-cells of step b) the subjects of step d) ? It is believed the former case is intended; see page 11, lines 6-7.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-7, 9, 11-12, 14-15, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotch et al (JEM 165, 408, 1987) alone or in view of McMicheal et al (JGV 67, 719, 1986).

Gotch et al teach assays which determine which components of influenza A virus are recognized by human CTL. Target cells are contacted with antigen (in the form of recombinant vaccine virus) in culture, in accord with claim 1, step a); See p. 409, last full paragraph. These target cells are then contacted with T-cells and a lytic T-cell response is determined, in accord with claim 1, steps b) and c); see paragraph spanning pages 409-410. Gotch et al determine which of the recombinant any antigen presented by the target cells are recognized by the CTL; see for example, pages 410-414. Gotch et al thus teach all of the in vitro steps of instant claim 1; they discuss the importance of developing vaccine in terms of providing components that are recognized by CTL; see paragraphs, spanning pages 408-409 and 412-413. Since it is art conventional, as admitted by applicant at specification pages 1-2, and as taught by McMichael et al (page 725 last paragraph), as well as required by the FDA, to test potential vaccines in vivo, it would have been obvious to further conduct in vivo experimental vaccinations with the components recognized by Gotch et al as targets of in vitro CTL. responses. Thus it would have been obvious to conduct all cited steps of claim 1.

Claim 11 is likewise rejected since the independent assay of the effects of multiple individual influenza A components with CTLs taught by Gotch et al is consistent with steps c) and d) of claim 11. For the same reason independent claim 14 is rejected.

Independent claim 18 is rejected since the mere determining of whether the CTL. responses are greater than a pre-selected value, such as a base line or background level, would have been conventional and hence obvious.

With respect to dependent claims. Claims 2-3, 12 and 15, note that the target cells and CTLs used by Gotch et al are human. See p. 409, last two full paragraphs.

Claim 4 is rejected since CTLs are inherently CD8 positive.

Claim 6 is included in the rejection since the EBV transformed lymphoblastoid target cells (p. 409 last full paragraph) would include B-cells.

Claim 7 is rejected since Gotch et al teach a lytic assay.

Claim 9 is included since any antigens recognized by CTL would inherently contain a T-cell epitope.

Claim 20 is rejected since Gotch et al teach that the target cells are autologous (p. 409, last full paragraph).

Claims 1, 6, 9, 11, 14, 18 and 20 are rejected under 35 U.S.C. 103(b) as being unpatentable over Sette et al (5,200, 320).

Sette et al teach screening of peptides for their binding to MHC receptors. Peptides that are identified as binding to MHC are selected for possible use in vaccines. Sette et al teach that

peptides selected for their binding property need to be further tested for immunogenicity, it is clear that the tests were conducted in vitro (with measurement of tritiated thymidine incorporation by proliferating T-cells; see col.9, lines 58-61). Sette et al teach that T-cells became activated when a trimolecular complex is formed of MHC on APCs, antigen, and T-cell receptor(see col. 1, lines 10-39 and col. 9, lines 12-15): thus their evaluation of peptide immunogencity must have inherently or would have obviously involved a presentation of antigenic peptide on APCs to the responding T-cells. Steps a) -c) of instant claim 1 thus would have been inherent or obvious in the method of Sette et al.

As noted supra, in the rejection stated over Gotch et al and McMicheal et al, in vivo testing of vaccines is art conventional and required by the FDA prior to FDA approval of any vaccine; hence further in vivo testing of peptides selected by the method of Sette et al, in accord with step d) of instant claim 1 would have been obvious.

Instant claims 11 and 14 are rejected, since Sette et al tested multiple peptides.

Claim 18 is rejected with the rational stated supra regarding Gotch et al and McMicheal et al.

Dependent calim 6 is rejected, since the APCs recited are conventional.

Claim 9 is rejected since the peptides selected by the methods of Sette et al must inherently contain a T-cell epitope, in order to be recognized by the T-cells.

Claim 20 is rejected, since Sette et al show peptides which bind to MHC and which stimulate T-cell proliferation in the same strain(s) of mice. See col.10, lines 10-25. Employing

APC and T-cells from the same in bred strain is functionally equivalent to employing autologous cells.

DWS 8/8/00

Claims ~~1-3, 5-9~~ 1-3, 5-9, 11-12, 14-15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baier et al (Jour of Virol, 69, 2357,1995).

Baier et al show an in vitro test of a vaccine composition. Various test immunogens are incubated with PBMC for 7 days. This step corresponds to steps a) and B) of claim 1. Following the incubation a T-cell response is determined by assaying for IL-2 secreted into the supernatant of the culture medium. This step corresponds to step c) of claim 1. See page 2359, col. 1 ; 2360, col. 1. See Figures 5 and 6. Thus all in vitro steps of claim 1 are shown.

Baier et al suggest further testing of the vaccine in non-human primates (page 2364). Thus the in vivo step of claim 1 is explicitly suggested, and as noted in rejections supra, such in vivo studies are art conventional and hence obvious.

Claims 11 and 14 rejected since Baier et al tested multiple potential antigens (e.g. Figs. 5 and 6), and since Baier et al suggest further testing of a potential vaccine giving a greatest response. Claim 18 is rejected for reasons stated supra with respect to Gotch et al.

Dependent claims 2-3, 12 and 15 are rejected since the PBMC culture containing APCS and T-cells are from human.

Claim 5 is rejected since the responding T-cells are CD4 positive (page 2362, col. 2).

Claim 6 is rejected since the PBMC culture would have included blood macrophage and B-cells.

Claims 7-8 are included since IL-2 is a cytokine.

Claim 9 is included because the vaccine include the epitopes (pages 2358, col. 1).

Claim 18 is included since each PBMC culture contain APCs and T cells from the same individual.

Claims 10, 13, 16-17 and 19 are not rejected over any of the above cited references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday through Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan , can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-3976.

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644

Saunders/Fisher

November 8, 1999